

IN THE CLAIMS

Please amend claims as follows.

1. (original) Method for the production of cyclic peptides, in which
 - a peptide cyclase is brought in contact with a linear peptide,
 - the linear peptide contains an acyl residue, which is activated by a nucleophilic leaving group bound chemically with this acyl residue,
 - the activated acyl residue of the linear peptide selectively acylates the center of the peptide cyclase, wherein the nucleophilic leaving group is cleaved off during formation of the cyclic peptide and
 - cyclic peptides with rings of at least 5 atoms are formed,wherein
 - the nucleophilic leaving group, which is chemically bound to the acyl residue of the linear peptide and which activates the latter, is charge-stabilized and
 - the charge-stabilized leaving group is bound to the acyl group of the C-terminal carboxylic acid group.
2. (currently amended) ~~Method~~ The method for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving groups are aromatic, heteroaromatic or araliphatic compounds, on which a hydroxy or thio group is bound to one of the ring atoms or to a carbon atom bound to the ring system.

3. (currently amended) ~~Method~~ The method for the production of cyclic peptides according to claim 1, wherein the peptide cyclase is a NRPS (non-ribosomal peptide synthetase) or PKS (polyketide synthetase) cyclase, preferably a purified, isolated thioesterase domain.

4. (currently amended) ~~Method~~ The method for the production of cyclic peptides according to claim 1, wherein the linear peptide contains proteinogenic and / or non-proteinogenic amino acids in its backbone, whereby residues which do not derive from amino acids can also be embedded in the backbone.

5. (currently amended) ~~Method~~ The method for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



wherein applies:

A [[= O, S]] is selected from O or S,

and whereby R1, R2, R3, R4 and R5 are independent of one another and are
selected from:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻,
-NL₂, -NH₂, -OL, -OH, -NHC(=O)L,
-OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl,
-cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl,
-heteroaryl,

wherein

L [[=]] is selected from: -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,
-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group
with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated
group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -
cycloalkyl and -cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl
stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms
chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic
groups group stands for a residue with 1 to 20 carbon atoms wherein up to 5 carbon
atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen,
sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms
and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon
atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen,
sulfur, and phosphorus.

6. (withdrawn) Method for the production of cyclic peptides according to claim 1,
wherein the charge-stabilized leaving group is a compound of the formula



wherein applies:

A = O, S

and whereby R1 and R2 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻,
-NL₂, -NH₂, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl, -
cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl,
-heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,
-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group
with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated
group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -
cycloalkyl and -cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl
stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms
chosen from the group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups

stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus.

7. (withdrawn) Method for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



wherein applies:

A = O, S and

Z = O, S,

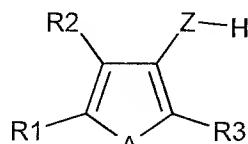
and whereby R1, R2, and R3 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻, -NL₂, -NH₂, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and -cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus.

8. (withdrawn) Method for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



(IV)

wherein applies:

A = O, S and

Z = O, S,

and whereby R1, R2, and R3 are independent of one another:

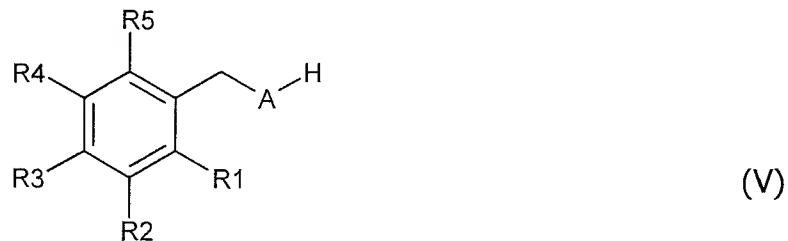
-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻,
-NL₂, -NH₂, -OL, -OH, -NHC(=O)L,
-OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl,
-cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl,
-heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,
-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group
with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated
group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -
cycloalkyl and -cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl
stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms
chosen from the group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups
stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are
substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur,
phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and
heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon

atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus.

9. (withdrawn) Method for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



wherein applies:

A = O, S

and whereby R1, R2, R3, R4 and R5 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺,

-NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻, -NL₂, -NH₂, -OL, -OH,

-NHC(=O)L, -OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl,

-cycloalkyl, -cycloalkenyl, -heteroalkyl,

-heterocycloalkyl, -aryl, -heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated

group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and -cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus.

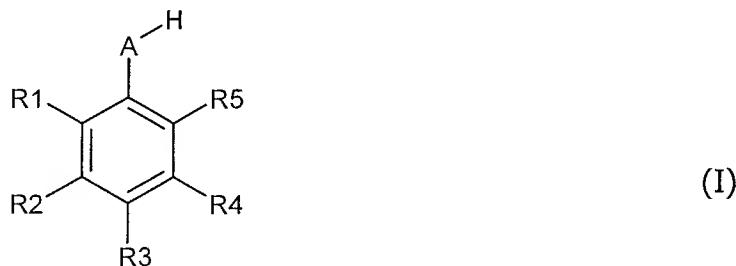
10. (currently amended) Method for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide, wherein the substrates are linear peptides, wherein the following steps are carried out one after the other:

- Adding adding a reagent activating the C-terminus of the peptide acid, a coupling additive and a charge-stabilized leaving group to the free peptide acid in a solvent
- Stirring stirring at room temperature,
- Addition adding of a base and further stirring at room temperature,
- Filtration filtering,
- Removal removing of the solvent,

- Deprotection deprotecting of the peptide,
- Addition adding of a peptide cyclase,
- Purification purifying of the cyclic peptide obtained
- wherein an acyl group of the C-terminal free peptide acid of the linear peptide is bound to the charge leaving group.

11. (withdrawn) Method for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 10, wherein the acyl group of the C-terminal amino acid of the linear peptide is bound to one of the charge leaving groups selected from the following:

a.) a compound of the formula



wherein applies:

A = O, S

and whereby R1, R2, R3, R4 and R5 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻, -NL₂, -NH₂, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl,

-cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl,

-heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group with

1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group

with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and

-cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an

alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the

group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue

with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by

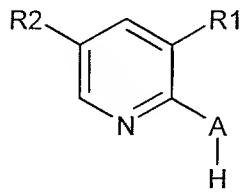
heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands

for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a

corresponding aromatic residue in which up to 5 carbon atoms are substituted by

heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus;

(b) a compound of the formula



(II)

wherein applies:

A = O, S

and whereby R1 and R2 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻, -NL₂, -NH₂, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and

-cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an

alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the

group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue

with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by

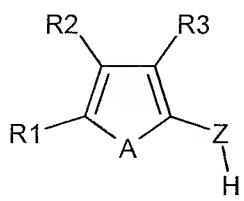
heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands

for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a

corresponding aromatic residue in which up to 5 carbon atoms are substituted by

heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus;

(c) a compound of the formula



(III)

wherein applies:

A = O, S and

Z = O, S,

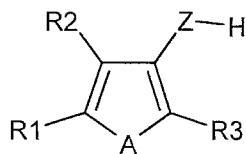
and whereby R1, R2, and R3 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻,
-NL₂, -NH₂, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl, -
cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl,
-heteroaryl,

wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,
-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group with
1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group
with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and
-cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an
alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the
group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue
with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by
heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands
for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a
corresponding aromatic residue in which up to 5 carbon atoms are substituted by
heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus;

(d) a compound of the formula



(IV)

wherein applies:

A = O, S and

Z = O, S,

and whereby R1, R2, and R3 are independent of one another:

-NO₂, -CN, -F, -Cl, -Br, -I, -CH₂Cl, -SO₃H, -H, -NH₃⁺, -NL₃⁺, -C(=O)L, -C(=O)Het, -O⁻,
-NL₂, -NH₂, -OL, -OH, -NHC(=O)L,
-OC(=O)L, -SL, -CO₂⁻, -alkyl, -alkenyl, -cycloalkyl,
-cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl,
-heteroaryl,

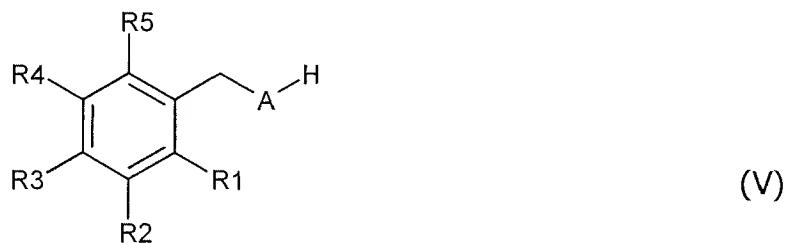
wherein

L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and -cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue

with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; and

(e) a compound of the formula



wherein applies:

$A = O, S$

and whereby $R1, R2, R3, R4$ and $R5$ are independent of one another:

$-NO_2, -CN, -F, -Cl, -Br, -I, -CH_2Cl, -SO_3H, -H, -NH_3^+,$
 $-NL_3^+, -C(=O)L, -C(=O)Het, -O^-, -NL_2, -NH_2, -OL, -OH,$
 $-NHC(=O)L, -OC(=O)L, -SL, -CO_2^-, -alkyl, -alkenyl,$
 $-cycloalkyl, -cycloalkenyl, -heteroalkyl,$
 $-heterocycloalkyl, -aryl, -heteroaryl,$

wherein

$L = -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,$
 $-heteroalkyl, -heterocycloalkyl, -aryl, -heteroaryl,$ wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and

—cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus.

12.(withdrawn) Method for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 11, wherein the leaving group possesses a pK_A value less than or equal to 10, preferably less than or equal to 8.

13.(withdrawn) Method for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 10, wherein DCC, DCI, PyClop, HBTU, HATU, HOSu, TBTU, T3P, BopCl or 3-Cl-1-pyridinium iodide are used as an activation reagent for the free C-terminus or a side chain carboxylic acid of the peptide carboxylic acid.

14. (withdrawn) Method for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 10, wherein HOBt, HOAt or HONB are used as a coupling additive.

15. (currently amended) A method Use of cyclic peptides according to claim 1 for the production of a pharmaceutical for the therapy, diagnosis and prophylaxis of diseases in which bacterial infections occur comprising using the cyclic peptides according to claim 1 for said production.

16. (currently amended) In a method of using [[Use of]] charge-stabilized leaving groups according to claim 1 in a kit for the production of cyclic peptides, the improvement comprising using the charge-stabilized leaving groups according to claim 1 in the kit.

17. (new) The method for the production of cyclic peptides according to claim 1, wherein the peptide cyclase is a purified, isolated thioesterase domain.